Message

From: Beck, Nancy [Beck.Nancy@epa.gov]

Sent: 12/11/2017 11:31:15 PM

To: Dourson, Michael [dourson.michael@epa.gov]

Subject: FW: Questions on epi studies

Attachments: Qs from OCSPP IO_draft_v2 .docx; Chlorpyrifos Data_Colu U.PDF; Appendix 6_2014 CPFOS HHRA.DOCX; Non-AChE

inhibition plausible AOPs from 2012 SAP white paper.docx; Whyatt and Rauh (2011).pdf

From: Keller, Kaitlin

Sent: Monday, December 11, 2017 2:53 PM

To: Beck, Nancy <Beck.Nancy@epa.gov>; Bertrand, Charlotte <Bertrand.Charlotte@epa.gov>

Subject: FW: Questions on epi studies

Nancy & Charlotte,

Attached are OPP's responses (and some supporting materials) to the chlorpyrifos epi study questions you had, below for reference. Let me know if you'd like hard copies.

- How were blood leads associated with the neurological outcomes independent of chlorpyrifos?
- If the chlorpyrifos metabolite is primarily made in the liver, and if this metabolite irreversibly binds to cholinesterase, then how does any of it get to the brain at concentrations in the blood that do not inhibit cholinesterase (~0.03 mg/kg-day from slide 23 of PBPK briefing on 11-15)?
- Experimental results in rats suggest that the fetus is less susceptible to cholinesterase inhibition than the dam. So why would human fetuses be more susceptible than their mothers?

Thanks, Kaitlin

Kaitlin Keller, Special Assistant Office of Chemical Safety and Pollution Prevention U.S. Environmental Protection Agency (202) 564-7098

From: Keigwin, Richard

Sent: Monday, December 11, 2017 9:30 AM **To:** Keller, Kaitlin < keller.kaitlin@epa.gov>

Cc: Lowit, Anna Lowit, Anna@epa.gov; Vogel, Dana Vogel, Dana <a href="https://www.

Reaves, Elissa < Reaves. Elissa@epa.gov>; Guilaran, Yu-Ting < Guilaran. Yu-Ting@epa.gov>; Friedman, Dana

<Friedman.Dana@epa.gov>; Smith, Charles <Smith.Charles@epa.gov>; Hughes, Hayley <hughes.hayley@epa.gov>; Tan,

Cecilia < Tan. Cecilia @epa.gov>; Padilla, Stephanie < Padilla. Stephanie @epa.gov>; Lobdell, Danelle

<Lobdell.Danelle@epa.gov>

Subject: FW: Questions on chlorpyrifos epi studies

Kaitlin-

Attached are responses to Nancy's questions as well as some additional supporting materials.

--Rick

From: Lowit, Anna

Sent: Friday, December 01, 2017 5:39 PM **To:** Keller, Kaitlin < keller, kaitlin@epa.gov>

Cc: Dinkins, Darlene < Dinkins. Darlene@epa.gov >; Keigwin, Richard < Keigwin. Richard@epa.gov >

Subject: RE: Questions on chlorpyrifos epi studies

Hi Kaitlin

These are not simple Qs & will take time to explain fully.

I've spent quite a bit of time today on this & definitely wont make early in the week. I need to have ORD & the OPP team provide comment on the responses. I also need a couple things out of the docket that I can't find—and Dana F is out of the office until Thursday. We are targeting Friday (8th) to get the responses to you.

Anna

Anna B. Lowit Senior Science Advisor

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US Environmental Protection Agency

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From: Keller, Kaitlin

Sent: Wednesday, November 29, 2017 10:51 AM

To: Lowit, Anna < Lowit. Anna@epa.gov>

Cc: Dinkins, Darlene < Dinkins, Darlene@epa.gov>; Keigwin, Richard < Keigwin, Richard@epa.gov>

Subject: Questions on chlorpyrifos epi studies

Hi Anna,

As discussed at the last chlorpyrifos briefing, the IO has a few follow up questions on the chlorpyrifos epi studies, listed below. Can we get answers by early next week?

- How were blood leads associated with the neurological outcomes independent of chlorpyrifos?
- If the chlorpyrifos metabolite is primarily made in the liver, and if this metabolite irreversibly binds to cholinesterase, then how does any of it get to the brain at concentrations in the blood that do not inhibit cholinesterase (~0.03 mg/kg-day from slide 23 of PBPK briefing on 11-15)?
- Experimental results in rats suggest that the fetus is less susceptible to cholinesterase inhibition than the dam. So why would human fetuses be more susceptible than their mothers?

Thanks, Kaitlin

Kaitlin Keller, Special Assistant Office of Chemical Safety and Pollution Prevention U.S. Environmental Protection Agency (202) 564-7098